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PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

INVENTOR(S)

Given Name (first and middle [if any])	Family Name or Surname	Residence (City and either State or Foreign Country)
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☐ *Additional inventors are being named on the____ separately numbered sheets attached hereto*

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TITLE OF THE INVENTION (280 characters max)

Topical Delivery of a Nitric Oxide Donor to Improve Skin Appearance

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ENCLOSED APPLICATION PARTS *(check all that apply)*

☒ Specification *Number of Pages* 31
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☐ Application Data Sheet. See 37 CFR 1.76
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METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT *(check one)*

☒ Applicant claims small entity status. See 37 CFR 1.27.
☐ A check or money order is enclosed to cover the filing fees
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☒ Payment by credit card. Form PTO-2038 is attached. Declined per Jeff Washville charge as a [illegible] 3/2/03

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The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.
☒ No.
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Respectfully submitted,

SIGNATURE [signature]

Date 20 FEB 04

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Docket Number: FOS-112

USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT

This collection of information is required by 37 CFR 1.51. The information is used by the public to file (and by the PTO to process) a provisional application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 8 hours to complete, including gathering, preparing, and submitting the complete provisional application to the PTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Mail Stop Provisional Application, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Topical Delivery of a Nitric Oxide Donor to Improve Body and Skin Appearance

Cross reference to related Applications

This application is a continuation-in-part of application no. 08/932,227 filed September 17, 1998, which is incorporated herein by reference in its entirety.

Background

Field of the Invention

This invention relates to improvement of the body and skin cosmetic appearance through the topical application of beneficial lotions or creams.

Prior Art

There have been many approaches to improving the body and skin appearance and consist of both systemic and topical approaches. One method of tightening skin to improve appearance is through the use of cosmetic surgery. The problems associated with this approach are obvious with the high cost and the risks associated with undergoing any medically unnecessary surgery. Radiofrequency energy is one method increasingly being used to tighten skin without the need for cutting as in a conventional facelift reducing some of the potential surgical

risks such as infection and anesthesia. This medical procedure is still troublesome to many individuals because it can cause damage to underlying tissues if not performed correctly.

Another surgical method to improve skin appearance of areas of the skin such as chins and arms is through liposuction. Liposuction is very effective for improving the appearance of skin, but it has a very high cost and there can be side effects such as infections that can lead to death.

The prior art treatment of skin without the use of cosmetic surgery involves many different treatments, but there are relatively few treatments that are actually effective in providing any noticeable benefits relative to the prohibitive costs. A popular method of providing the appearance of a tightening of the skin is to remove small wrinkles through the use of alpha lipoic acid. This does not cause much of a tightening effect only the removal of tiny wrinkles providing the appearance of tightening. Although almost any treatment can produce a negative reaction in a some people, adverse reactions to lipoic acid are less common than to such agents as Retin A, vitamin C or glycolic acid. Alpha lipoic acid is useful in treating small wrinkles but it can result in rashes because of a reaction to the acid. For sagging skin, larger wrinkles or double chins the individual normally has to resort to cosmetic

surgery commonly known as a facelift or a tuck. Sagging breasts have also been treated surgically.

The instant invention addresses treatment of body and skin to improve appearance without resorting to the risks and expense of surgery. Furthermore the instant invention is effective while addressing and overcoming the negative side effects of other known prior art topical skin treatments.

Summary of the Invention

The invention provides beneficial cosmetic effects in appearance to body and skin, by smoothing skin that is wrinkled, sagging, or cellulite-afflicted by the application of a cream, liquid or transdermal patch containing a nitric oxide donor in a sufficient concentration to improve the appearance of a selected area of the body. The nitric oxide donor is at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase.

The cream treats the appearance of double chins, crows feet and a multitude of other cosmetic problems associated with wrinkled, sagging or dimpled appearance that affect the smoothness of the surface of the skin. The appearance of sagging skin that may occur on breasts, arms, legs, back,

ankles, stomach, "love handles" and buttocks can be treated to produce a more desirable appearance by applying the cream or liquid containing the effective ingredients. In one embodiment the nitric oxide donor is L-arginine or its derivatives in a quantity sufficient to produce the desired cosmetic effects.

In another embodiment of the invention, a penetrating cream containing nitric oxide donor such as L-arginine or its derivatives, at an effective concentration, along with other substances to create a hostile biophysical environment for absorption of the nitric oxide donor such as L-arginine into to the skin is provided to produce cosmetic benefits. In this embodiment an agent or agents is combined with a sufficient concentration of a nitric oxide donor such as L-arginine is provided in the penetrating cream to create the hostile biophysical environment.

Accordingly, several objects and advantages of the instant invention are to remove small wrinkles by means of enhancement of the body's natural mechanisms.

It is yet another object of the instant invention to remove the appearance of the condition commonly known as a "double chin" by means of enhancement of the body's natural mechanisms.

It is still another object of the instant invention to tighten sagging breasts by means of enhancement of the body's own natural mechanisms.

Another object is to smooth cellulite-afflicted skin by means of enhancement of the body's own natural mechanisms.

It is still further an object of the instant invention to smooth facial tissue without surgery by means of enhancement of the body's own natural mechanisms.

Another object is to lift sagging arm tissue by means of enhancement of the body's own natural mechanisms.

Another object is to lift and tighten sagging buttocks by means of enhancement of the body's own natural mechanisms.

A further object is to lift and tighten sagging leg skin by means of enhancement of the body's own natural mechanisms.

These and other objects and features of the present invention will become apparent to those skilled in the art from reading the description of the invention, which follows.

Detailed Description of the Invention

The invention consists of a base cream, liquid, lotion or transdermal patch that promotes transfer into the skin an effective concentration nitric oxide either directly or through a nitric oxide donor capable of penetration into the substrate underlying the skin. The application of nitric oxide improves

the cosmetic appearance of the skin through a smoothing and tightening effect caused by natural biological responses to the presence of nitric oxide. A nitric oxide donor is a compound that contains a nitric oxide moiety and releases or chemically transfers nitric oxide to another molecule either directly or through a biological process into the skin and tissues such as muscles and the elements of the circulatory system in close proximity to the surface of the skin.

In one embodiment the nitric oxide is provided by a concentration of at least 0.75% by weight of L-arginine with effective penetrating agents, or at least 10% by weight of L-arginine or its derivatives without the use of penetrating agents for application to skin having a wrinkled, sagging or cellulite afflicted appearance.

When a nitric oxide donor such as L-arginine is combined with a sufficient quantity of agent or agents in a penetrating cream an effective concentration of L-arginine is at least 0.75% w/v.

It was discovered that topical application of a nitric oxide precursor, L-arginine, in its various forms contained in a variety of topical preparations, either by themselves or with other agents to aid in penetration, such as a high ionic strength environment, neutralization of its charge in a complex or by other means, or included in a liposome or other biological

carrier, when administered to the skin causes a beneficial cosmetic effect to the area of the skin applied. Other nitric oxide donors may be substituted to create the skin smoothing and appearance improvement.

Further, in accordance with this invention, a penetrating cream containing L- arginine or its derivatives in a concentration sufficient to produce the desired effect at a concentration sufficient to produce a hostile biophysical environment when applied to skin induces firmness, smoothness and removes sagging appearance of skin and body parts such as breasts within a short period after application with the effect lasting several hours. Further repetitive daily treatments increase the duration of the beneficial effects on appearance after application with the benefits lasting up to a period of twenty hours. The concentration of L-arginine or its derivatives can be reduced to maintain the same desired duration of cosmetic effect.

In another embodiment, the delivery vehicle is a penetrating cream, the L- arginine is present as L-arginine hydrochloride in a concentration sufficient to produce the desired effect and the penetration agents that creates the hostile biophysical environment are ionic salts which is selected from the group consisting of sodium chloride, magnesium chloride, calcium chloride, choline chloride or combinations

thereof at a concentration sufficient to aid in tissue absorption of the L-arginine.

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Alternatively, in another embodiment, a nitric oxide donor can be substituted to include polysaccharide-bound nitric oxide-nucleophile adducts as described in U.S. Patent **5,691,423**, the contents of which are incorporated by reference. A polymeric composition capable of releasing nitric oxide, in a controlled manner for effective dosing, comprises a polysaccharide including a nitric-oxide releasing N2O2- functional group bound to the polymer. These molecules are lipophilic, biodegradable, biocompatable, and degrade into naturally occurring products. The nitric oxide release also provides the beneficial cosmetic

effects when applied in an effective concentration.

Another embodiment is the application of N-nitroso-N-substituted hydroxylamines for use as nitric oxide donors as described in U.S. patent 5,698,738, the contents of which are incorporated by reference. This nitric oxide donor is a NONOate anion linked to an ortho-substituted aryl, a heteroaromatic substituent, asteroid, or a catecholamine. Preferred ortho substituents are alkoxy, halo, and alkyl. The cation of the salt is an alkali metal, an alkaline-earth metal, an ammonium or substituted ammonium group. Nitric oxide donors provided herein are more stable than that of nitrogen-bonded NONOates described previously. The by product left after release of NO, and the nitric oxide donors themselves, are very probably less carcinogenic than the corresponding nitrogen-bonded NONOates. Examples of nitric oxide donors in this embodiment are as follows:

N-Nitroso-N-(1-naphthyl)-hydroxylamine, ammonium salt (neocupferron)
Idem, sodium salt (via ionic exchange, from the preceding compound).
N-Nitroso-N-(2-methylphenyl)-hydroxylamine, salt
N-Nitroso-N-(2-methoxyphenyl)-hydroxylamine, salt
N-Nitroso-N-(2-ethylphenyl)-hydroxylamine, salt
N-Nitroso-N-(2-isopropylphenyl)-hydroxylamine, salt
N-Nitroso-N-(2,4-difluorophenyl)-hydroxylamine, salt
N-Nitroso-N-(2,5-difluorophenyl)-hydroxylamine, salt
N-Nitroso-N-(2-chlorophenyl)-hydroxylamine, salt
N-Nitroso-N-(2,3-dichlorophenyl)-hydroxylamine, salt
N-Nitroso-N-(2,4-dichlorophenyl)-hydroxylamine, salt
N-Nitroso-N-(2,5-dichlorophenyl)-hydroxylamine, salt
N-Nitroso-N-(2-bromophenyl)-hydroxylamine, salt
N-Nitroso-N-(5-fluoro-2-methylphenyl)-hydroxylamine, salt
N-Nitroso-N-(4-fluoro-2-methylphenyl)-hydroxylamine, salt
N-Nitroso-N-(4-choro-2-methylphenyl)-hydroxylamine, salt
N-Nitroso-N-(3-choro-2-methylphenyl)-hydroxylamine, salt

In another embodiment the nitric oxide donor is a compound containing a sulfhydryl group and a NO donor group, wherein said compound contains an acetylated sulfhydryl group linked to an aromatic ring or a heteroaromatic ring with a nitrogen in the ring structure, which ring is substituted by a substituent bearing a terminal -ONO. This is described in U. S. patent 6,642,260, the contents are incorporated by their entirety. Specific useful compounds for nitric oxide donation similar to the effectiveness of nitroglycerin are trans-1,2-Dinitrato-4,5-dithiane; 2,2'-Dithiodiethanol-dinitrate; 1,1-Diemethanol-dinitrate-3,4-dithiane; 1,1'-Bisthiomethyl-3,4-dihydroxy-cyclohexane-dinitrate ester; Thiotyl Alcohol Nitrate Ester; 1,2-Dihydroxy-dinitrate-6,8-dithiane.

In another embodiment another compound useful for nitric oxide donation is 1,3-(nitrooxymethyl)phenyl 2-hydroxybenzoate and other related donors as described in U.S. Patent 6,538,033, the contents of which are incorporated by reference.

In another embodiment to provide nitric oxide is described in U.S. Patent No. 6,103,275, herein incorporated by reference in its entirety, by topically applying first gel comprising a nitrite salt, and a biocompatible reductant and a second gel comprising an acid with a pKa between about 1 and about 4 to a body site in an amount effective to enhance local blood flow.

In another embodiment the nitric oxide is provided by a chitosan-based polymeric nitric oxide donor composition as described in U.S. patent 6,451,337, the contents are incorporated by their entirety.

In another embodiment nitric oxide donors are described in U.S. Patent no. 6,617,337 are herein incorporated by reference. The nitric oxide donors can be selected from the group consisting of sodium nitroprusside (Nipride), S-nitrosoacetylpenacillamine (SNAP), 3-morpholino-synonimin-hydrochloride (SIN-1), 3-morpholino-N-athoxycarbonyl-sydnonimin (molsidomin), amyl nitrite (isoamyl nitrite), nitroglycerin (glyceryl trinitrite), isosorbide dinitrate (Isodil), isosorbide-5-mononitrite (Imur), and erythrityl tetranitrate (cardilate).

In another embodiment an effective dose of nitric oxide is provided by nitric oxide-releasing amidine- and enamine-derived diazeniumdiolates, compositions comprising such compounds. These compounds are taught in U.S. Patent no. 6,511,991, the contents of which are incorporated herein in their entirety.

In another embodiment the source of nitric oxide is piperidine and pyrrolidine derivatives comprising a nitric oxide donor. These compounds are described in U.S. Patent no. 6,448,267, the contents of which are incorporated by reference in their entirety.

In another embodiment the cream contains L-arginine or its derivatives, and it is combined with agents that aids penetration. The effective range of L-arginine or its derivatives is about 0.1 to 25% w/v when used in conjunction with an effective concentration of penetrant aid. The concentration of L-arginine in the cream can be reduced with the inclusion of a greater amount or concentration of penetration aids or increased to lengthen the beneficial cosmetic effect. The concentration of L-arginine when combined with an effective penetration aid is preferably at least about 5% w/v or greater.

In one embodiment the cream contains the L-arginine derivative of L-arginine hydrochloride with at least 12.5% weight by volume, and is combined with choline chloride having at least 10% weight by volume, sodium chloride with at least 5% weight by volume, and magnesium chloride with at least 5% weight by volume. The optional additional components of the base cream may be water, mineral oil, glyceryl stereate, squalene, propylene glycol stearate, wheat germ oil, glyceryl stearate, isopropyl myristate, steryl stearate, polysorbate 60, propylene glycol, oleic acid, tocopherol acetate, collagen, sorbitan stearate, vitamin A & D, triethanolamine, methylparaben, aloe vera extract, imidazolidinyl urea, propylparaben, pnd BHA or any combination thereof.

L-arginine hydrochloride provides a precursor to the molecule, nitric oxide, NO. Nitric oxide is the substance that relaxes the blood vessels, allowing for increased blood flow. Choline chloride, sodium chloride and magnesium chloride provides a high ionic strength environment for the highly charged molecule, L-arginine. This high ionic strength environment is an example of a hostile biophysical environment for L-arginine. That is, the highly charged ionic strength is an unfavorable environment for the highly charged L-arginine making the L-arginine anxious to move to a more hospitable, less charged environment such as human tissue. The base cream containing L-arginine, choline chloride, sodium chloride and magnesium chloride is the agent that produces beneficial cosmetic effects such as removing wrinkles, reducing sagging and smoothing cellulite afflicted skin.

Other Embodiments -Other active agents

While L-arginine hydrochloride is the preferred active agent because it is the agent in nature itself, it is non-toxic, is highly soluble and it is inexpensive, other agents could be used which are also precursors or donors of nitric oxide. These include D,L -arginine, L-arginine, alkyl (ethyl, methyl, propyl, isopropyl, butyl, isobutyl, t- butyl) esters of L-arginine and salts thereof as well as other derivatives of arginine and other

nitric oxide donors. Pharmaceutically acceptable salts include hydrochloride, glutamate, butyrate, and glycolate. Other similar compounds for direct substitution for L-arginine are L-homoarginine, N-hydroxy-L-arginine, nitrosated L-arginine, nitrosylated L-arginine, nitrosated N-hydroxy-L-arginine, nitrosylated N-hydroxy-L-arginine, citrulline, omithine, linsidomine, nipride or glutamine.

In the case of an alternative active agent were used it would be simply substituted for L-arginine in a delivery preparation and the preparation used as in the case of the L-arginine preparation.

A nitric oxide donor is a compound that contains a nitric oxide moiety and which releases or chemically transfers nitric oxide to another molecule. Nitric oxide donors include but are not limited to S-nitrosothiols, nitrites, 2-hydroxy-2-nitrosohydrazines, and substrates of various forms of nitric oxide synthase. Compounds that stimulate endogenous production of nitric oxide or EDRF in vivo include L-arginine, the substrate for nitric oxide synthase, cytokines, adenosine, bradykinin, calreticulin, bisacodyl, phenolphthalein, OH-arginine, and endothelein.

Other Means of Effecting or Improving Absorption

A variety of means for effecting or improving absorption of the active agent can be envisioned. One principle behind the absorption of a highly charged molecule such as L-arginine into tissue is to either create a biophysically hostile environment in the delivery vehicle such that L-arginine would prefer to be in tissue, or to package L-arginine in such a way that it is carried into tissue or neutralize its charge by derivitization or forming a neutral salt. Examples of biophysically hostile environments, include but are not limited to; high ionic strength by the addition of ionic salts such as sodium chloride, magnesium chloride or choline chloride; high or low pH by adding pharmaceutically acceptable acids or bases; and highly hydrophobic environments by decreasing water content and increasing lipid, oil and/or wax content. Examples of packaging which would be carried into tissue includes liposomes or emulsions of collagen, collagen peptides or other components of skin or basement membrane. Examples of neutralization of charge include delivery of the active agent in the form or an ester or salt such as arginine glutamate, which is electronically neutral.

In each case of creating a hostile biophysical environment for the active agent, the agent was added to an appropriate preparation. In the case of creating a high ionic strength ions

such as but not limited to sodium chloride, potassium chloride, choline chloride, magnesium chloride, lithium chloride, alone or in combination were added in high concentration. Other highly charged molecules such as polylysine, polyglutamine, polyaspartate or copolymers of such charged amino acids may be used to create the hostile biophysical environment.

Alternatively a hostile biophysical environment may be created by placing the highly charged L-arginine in an hydrophobic, oily environment such as in an oil-based cream containing little or no water. Absorption may further be aided by combining the use of hostile biophysical environments with the use of penetrating agents such as oleoresin capsicum or its constituents or molecules containing heterocyclic rings to which are attached hydrocarbon chains.

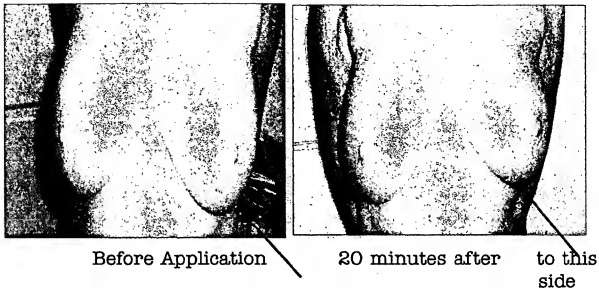
Reduction of breast sagging and increase of breast firmness

Example 1

In this example a 60-year-old woman with pendulous breasts was provided with a penetrating cream comprising L-arginine (12.5% w/v), sodium chloride (10% w/v) and magnesium chloride (5% w/v). The cream was applied to one of the breasts, which was rubbed in extensively for maximal absorption. After a period of approximately 20 minutes the treated breast was much

fuller and raised up by about 1.5 inches. The effect of the initial treatment lasted for a period of about seven hours.

The concentration of L-arginine can be reduced to decrease the duration of the cosmetic effect of the initial application. The minimum effective concentration of L-arginine or its derivatives is about at least 0.5% w/v, but it is preferably a greater initial treatment amount otherwise the initial duration of the cosmetic benefit will be too brief. The concentration of L-arginine is tailored to have a duration of at least 3 hours, preferably 8 or more. This is dependent upon the concentration of penetration aid used in conjunction with the L-arginine. The concentration to produce a beneficial cosmetic effect during initial application, of at least 3 hours, is at least 5%.



The transdermal L-Arginine cream was applied to the breast indicated by completely covering the breast with cream. The cream was then rubbed into the breast for 5 min. The second picture was taken 20 min. after application was complete.

Example 2

In this example a 47-year-old woman with extremely pendulous breasts applied a breast lifting cream comprising L-arginine (12.5% w/v), choline chloride (10% w/v), sodium chloride (10% w/v) and magnesium chloride (5% w/v). The breast lifting creaming was rubbed vigorously into each breast for about five minutes. Within one hour both breasts were noticeably firmer and had been lifted about 2.75 inches. The effect of the initial treatment lasted for about five hours.

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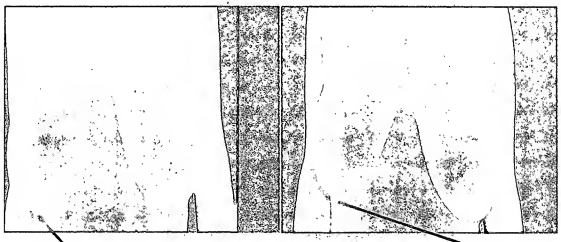
The treatment was continued daily for about a month. The lifting effect of the treatment had an effective duration of about eighteen to twenty hours after a month of daily use.

The concentration of L-arginine can be maintained to continue cosmetic benefits for up to twenty hours if the same cream is applied on a regular basis of once every 8 to 48 hours, preferably every 12-36 hours.



The transdermal L-Arginine cream was applied to the breast indicated by completely covering the breast with cream. The cream was then rubbed into the breast for 5 min. The second picture was taken 20 min. after application was complete

Improving the Appearance of Neck and Chin

CHINS

A 59 yr old woman with a large "double chin" applied a chin lifting cream consisting of a delivery vehicle of penetrating cream, L-arginine (12.5% w/v), sodium chloride (10% w/v) and magnesium chloride (5% w/v) to the tissue of her chin and under

her chin by completely covering the area with the cream and rubbing it in for 5 minutes. After 15 minutes she looked in the mirror and observed that the "double chin" was completely gone and the skin on and under her chin was extremely smooth. The concentration of L-arginine can be changed to lengthen or shorten duration of cosmetic benefits as discussed above.

Reduction of Wrinkles

FACIAL TISSUE

A 64 yr old woman with extremely saggy wrinkled facial tissue applied a face lifting cream consisting of a delivery vehicle of penetrating cream, L-arginine (12.5% w/v), sodium chloride (10% w/v) and magnesium chloride (5% w/v) to her entire face (taking care to avoid the eyes) by completely covering the area with cream and rubbing it in for 5 minutes. Within 30 minutes she noticed the sagging facial tissue was substantially lifted and much smoother. The effect lasted for 14 hours. She continued the treatment daily for two weeks and at the end of the two weeks the treatment left her facial skin completely devoid of sagging tissue and it was completely smooth. The effect persisted for 14-16 hours.

Lifting of Sagging Skin Tissue

BUTTOCKS

A 160 lb. 55 yr old woman with flabby and sagging buttocks applied a buttock lifting cream consisting of a delivery vehicle of penetrating cream, L-arginine (12.5% w/v), sodium chloride (10% w/v) and magnesium chloride (5% w/v) to her buttocks by completely covering them with cream and rubbing the cream in for 5 minutes. She looked in the mirror in one hour and observed that the sagging was substantially reduced and that the buttocks were more firm. She continued the treatment daily for one month. At the end of the month her buttock sag was completely gone after application of the cream and they were firm and youthful. The effect persisted throughout the day.

UNDER ARM and LEG TISSUE

A 72 yr old man with sagging tissue on the bottom of his upper arms and in his lower legs applied an arm and leg lifting cream consisting of a delivery vehicle of penetrating cream, L-arginine (12.5% w/v), sodium chloride (10% w/v) and magnesium chloride (5% w/v) to his upper arms and lower legs by completely covering them with cream and rubbing the cream in for 5 minutes. After one hour the sagging tissue was substantially lifted up and firmed. The effect persisted for 7 hours. He continued the treatment of his arms and legs daily for one week. At the end of

the week the treatment resulted in youthful looking arms and legs with the sag completely reversed. The effect lasted 11-17 hours.

Although the description above contains many specificities, these should not be construed as limiting the scope of the invention but as merely providing illustrations of some of the presently preferred embodiments of this invention. Various other embodiments and ramifications are possible within this scope. Thus the scope of the invention should be determined by the appended claims and their legal equivalents, rather than by the examples given.

I claim:

1. A method of treating sagging skin comprising the steps of:
   a) selecting a section of sagging skin;
   b) applying a lotion containing an effective concentration of a nitric oxide donor into the sagging section of skin to reducing visual appearance of sagging;
   c) rubbing the lotion until absorbed into the skin.

2. The method of claim 1 wherein the sagging section of skin is selected from the group consisting of chins, necks, face, forehead, arms, legs, buttocks, and ankles.

3. The method of claim 1 wherein the effective concentration of nitric oxide donor is L-arginine at least 5% percent by weight/volume of the lotion.

4. The method of claim 2 wherein the lotion further comprises additives selected from the group consisting of water, mineral oil, glyceryl stereate, squalene, propylene glycol stearate, wheat germ oil, glyceryl stearate, isopropyl myristate, steryl stearate, polysorbate 60, propylene glycol, oleic acid, tocopherol acetate, collagen, sorbitan stearate, vitamin A & D, triethanolamine, methylparaben, aloe vera extract,

imidazolidinyl urea, propylparaben, pnd BHA and combinations thereof.

5. The method of claim 4 wherein the lotion contains a penetrating agent wherein an effective concentration of L-arginine is at least 2.5% by weight of the lotion and the cosmetic benefits lasts at least 3 hours after initial treatment.

6. The method of claim 1 further comprising the step of:

c) reapplying the lotion containing an effective concentration of an L-arginine based compound 8 to 36 hours after the first application to the same selected section of skin.

7. The method of claim 5 further comprising the steps of:

c) reapplying the lotion containing an effective concentration of an L-arginine based compound 8 to 36 hours after the first application to the same selected section of skin.

d) repeating step C about 2 to 30 times within a time period of one month.

8. The method of claim 7 wherein the means of aiding penetration is an ionic salt having a concentration of at least 5% by weight/volume of the lotion.

9. The method of claim 8 wherein the ionic salt is selected from the group consisting of at least 10% by weight of sodium chloride, at least 10% by weight of magnesium chloride, at least 10% by weight of choline chloride and combinations thereof.

10. The method of claim 1 wherein the nitric oxide donor is selected from the group consisting of polysaccharide-bound nitric oxide-nucleophile adducts, N-nitroso-N-substituted hydroxylamines, a compound containing a sulfhydryl group and a NO donor group, 1,3-(nitrooxymethyl)phenyl 2-hydroxybenzoate, nitrite salt and acid, S-nitrosothiols, nitrites, 2-hydroxy-2-nitrosohydrazines, and substrates of various forms of nitric oxide synthase, the substrate for nitric oxide synthase, cytokines, adenosine, bradykinin, calreticulin, bisacodyl, phenolphthalein, and endothelein.

10. A method of improving the appearance of skin affected by cellulite, wrinkles or sagging by smoothing comprising the steps of:

a) selecting an area of skin requiring cosmetic smoothing to improve the appearance of wrinkles, cellulite or sagging;

b) applying a carrier containing an effective concentration of a nitric oxide means to the selected section of skin until a sufficient quantity of nitric oxide is absorbed to produce smoother skin in the selected area.

11. The method of claim 10 wherein the carrier is a lotion that further comprises additives selected from the group consisting of water, mineral oil, glyceryl stereate, squalene, propylene glycol stearate, wheat germ oil, glyceryl stearate, isopropyl myristate, steryl stearate, polysorbate 60, propylene glycol, oleic acid, tocopherol acetate, collagen, sorbitan stearate, vitamin A & D, triethanolamine, methylparaben, aloe vera extract, imidazolidinyl urea, propylparaben, pnd BHA and combinations thereof.

12. The method of claim 10 further comprising the step of:

D) reapplying the lotion containing an effective concentration of the nitric oxide means at least once every 8 to 48 hours after the first application to the same selected section of skin to increase the duration of the smoothing effect upon the skin.

13. The method of claim 10 wherein the effective concentration of the nitric oxide means is provided by L-arginine having at least 10% by weight/volume of the carrier.

14. The method of claim 10 wherein the lotion further comprises a means of aiding penetration.

15. The method of claim 14 wherein an effective concentration of L-arginine is at least 2.5% by weight/volume of the lotion.

16. The method of claim 15 wherein the means of aiding penetration is an ionic salt.

17. The method of claim 16 wherein the penetrating agent is an ionic salt selected from the group consisting of sodium chloride, choline chloride, magnesium chloride, or a combination thereof.

18. The method of claim 16 wherein the ionic salt has a concentration of at least 5%.

19. The method of claim 17 wherein the penetrating agent comprises at least 10% by weight/volume of sodium chloride and at least 10% by weight/volume of magnesium chloride.

20. A compound for tightening and smoothing skin or lifting sagging body parts comprising:

a lotion or cream for topical application comprising an effective concentration of at least 5% by weight/volume of an L-arginine based compound;

a penetrating means comprising an effective concentration of at least 5% by weight/volume.

21. A compound for tightening or smoothing skin and lifting sagging body parts comprising:

a means of providing nitric oxide: and,

an additional agent, wherein said agent is selected from the group consisting of water (20-80%), white oil (3-18%), glyceryl stearate (0.25-12%) squalene (0.25-12%), cetyl alcohol (0.1-11%), propylene glycol stearate (0.1-11%), wheat germ oil (0.1-6%), polysorbate 60 (0.1-5%), propylene glycol (0/05-5%), collagen (0.05-5%), sorbitan stearate (0/05-5%) vitamin A&D (0/02-4%), vitamin E (0.02-4%), triethanolamine (0.01-4%), methylparaben (0.01-4%), aloe vera extract (0/01-4%), imidazolidinyl urea (0.01-4%) propylparben (0.01-4%), bha 0.01-4%), L-Arginine Hydrochloride (0.25-25%), sodium chloride (0.25-25%), magnesium chloride (0.25-25%), and combinations thereof.

22. The compound in claim 21 wherein the cream further contains choline chloride (0.25-25%).

23. The compound in claim 21 in which L-Arginine glutamate is (02.5-25%) substituted for L-Arginine Hydrochloride.

24. A method of improving skin appearance comprising the steps of:

selecting a section of skin;

applying a carrier vehicle containing an effective concentration of a means of producing a nitric oxide into the section of skin to improve visual appearance.

25. The method of claim 24 further comprising the steps of:

selecting a lotion as the carrier vehicle; and,

rubbing the lotion until absorbed into the skin.

26. The method of claim 25 further comprising the step of:

reapplying the lotion containing an effective concentration of the nitric oxide means at least once every 8 to 48 hours after the first application to the same selected section of skin to increase the duration of the improved visual appearance.

ABSTRACT

A preparation is disclosed for producing enhanced cosmetic appearance to sagging, wrinkled or cellulite afflicted areas of the skin and body. Specifically, this is a preparation, which provides local delivery of Nitric oxide, in one embodiment the nitric oxide is produced by the amino acid L- arginine, an important biological precursor is provided so that it can be topically applied to the area requiring cosmetic treatment. The preparation may also contain an agent, which aids in the transfer of the Nitric oxide donor into the tissue and overcomes the resistance to transfer into the skin. High ionic strength is created by addition of choline chloride, magnesium chloride and sodium chloride aids in penetration.